# NMCP COVID-19 Literature Report #81: Friday, 19 November 2021

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**Purpose:** These reports, published every other week on Fridays, are curated collections of current research, evidence reviews, special reports, grey literature, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers.

All reports are available online at <a href="https://nmcp.libguides.com/covidreport">https://nmcp.libguides.com/covidreport</a>. Access is private; you will need to use the direct link or bookmark the URL.

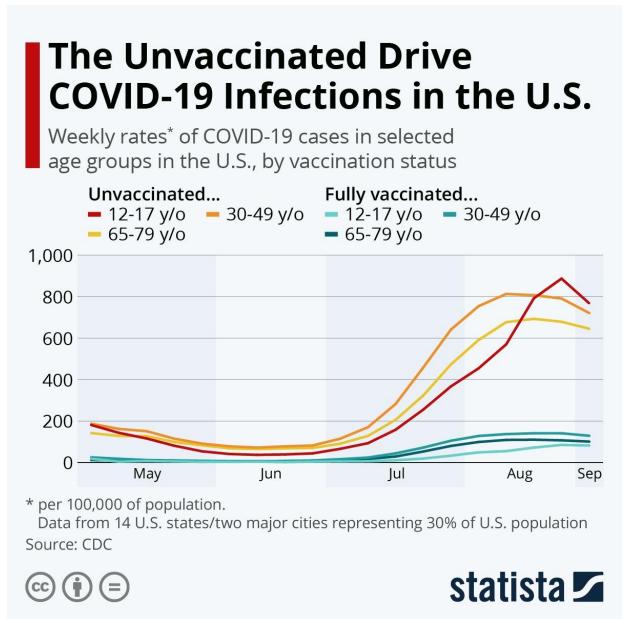
**Disclaimer:** I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Please feel free to reach out with questions, suggestions for future topics, or any other feedback.

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*supplement* 

### The Big Picture



Source: https://www.statista.com/chart/26159/covid-cases-us-age-group-vaccination-status/

### **News in Brief**

The pandemic's next turn hinges on three unknowns — a potential winter surge is up to vaccines, variants, and us" (Atlantic).

"'Zero-Covid is not going to happen': experts predict a steep rise in US cases this winter — Total US deaths from Covid may reach 1 million by spring as vaccination rates remain lower than 60%" (Guardian).

#### More Waves

"Not all Covid waves look the same. Here's a snapshot of the Delta surge" (STAT).

It looks like the 5th wave is hitting Europe (CIDRAP; see also: Reuters article about France).

"Europe's COVID death toll could rise by hundreds of thousands — In a worst-case scenario, the pandemic could cause a further 300,000 deaths if anti-contagion policies are lifted and people revert to their old habits" (Nature).

Meanwhile... "U.S. CDC raises COVID-19 travel warnings for Czech Republic, Hungary" (Reuters).

### Journal Articles

MMWR: <u>Impact of Hospital Strain on Excess Deaths During the COVID-19 Pandemic — United States</u>, <u>July 2020–July 2021</u> (19 November 2021)

"What is already known about this topic? COVID-19 surges have stressed hospital systems and negatively affected health care and public health infrastructures and national critical functions.

What is added by this report? The conditions of hospital strain during July 2020—July 2021, which included the presence of SARS-CoV-2 B.1.617.2 (Delta) variant, predicted that intensive care unit bed use at 75% capacity is associated with an estimated additional 12,000 excess deaths 2 weeks later. As hospitals exceed 100% ICU bed capacity, 80,000 excess deaths would be expected 2 weeks later.

What are the implications for public health practice? State, local, tribal, and territorial leaders could evaluate ways to reduce strain on public health and health care infrastructures, including implementing interventions to reduce overall disease prevalence such as vaccination and other prevention strategies, and ways to expand or enhance capacity during times of high disease prevalence."

Lancet: <u>How an outbreak became a pandemic: a chronological analysis of crucial junctures and international obligations in the early months of the COVID-19 pandemic (08 November 2021)</u>

"Understanding the spread of SARS-CoV-2, how and when evidence emerged, and the timing of local, national, regional, and global responses is essential to establish how an outbreak became a pandemic and to prepare for future health threats. With that aim, the Independent Panel for Pandemic Preparedness and Response has developed a chronology of events, actions, and recommendations, from December, 2019, when the first cases of COVID-19 were identified in China, to the end of March, 2020, by which time the outbreak had spread extensively worldwide and had been characterised as a pandemic. Datapoints are based on two literature reviews, WHO documents and correspondence, submissions to

the Panel, and an expert verification process. The retrospective analysis of the chronology shows a dedicated initial response by WHO and some national governments, but also aspects of the response that could have been quicker, including outbreak notifications under the International Health Regulations (IHR), presumption and confirmation of human-to-human transmission of SARS-CoV-2, declaration of a Public Health Emergency of International Concern, and, most importantly, the public health response of many national governments. The chronology also shows that some countries, largely those with previous experience with similar outbreaks, reacted quickly, even ahead of WHO alerts, and were more successful in initially containing the virus. Mapping actions against IHR obligations, the chronology shows where efficiency and accountability could be improved at local, national, and international levels to more quickly alert and contain health threats in the future. In particular, these improvements include necessary reforms to international law and governance for pandemic preparedness and response, including the IHR and a potential framework convention on pandemic preparedness and response."

Soc Sci Med: <u>Modeling epidemic recovery: An expert elicitation on issues and approaches</u> (06 November 2021)

"Since the emergence of the SARS-CoV-2 virus in late 2019, the world has been in a state of high alert and reactivity. Once the acute stage of the infectious disease crisis does abate, however, few if any communities will have a detailed roadmap to guide recovery – that is, the process of becoming whole again and working to reduce similar, future risk. In both research and policy contexts where data are absent or difficult to obtain, expert judgment can help fill the void. Between November 2019 and February 2020, we conducted an expert elicitation process, asking fourteen key informants – with specializations in infectious diseases, disaster recovery, community resilience, public health, emergency management, and policymaking – to identify the design principles, priority issues, and field experiences that should inform development of an epidemic recovery model. Participants argued that recovery from epidemics is distinct from natural disasters due to epidemics' potential to produce effects over large areas for extended periods of time and ability to generate high levels of fear, anticipatory anxiety, and antisocial behavior. Furthermore, epidemic recovery is a complex, nonlinear process involving many domains – political, economic, sociocultural, infrastructural, and human health. As such, an adequate model of post-epidemic recovery should extend beyond strictly medical matters, specify units of interest (e.g., individual, family, institution, sector, community), capture differing trajectories of recovery given social determinants of health, and be fit for use depending upon user group (e.g., policymakers, responders, researchers). This formative study commences a longer-term effort to generate indicators for a holistic, transformative epidemic recovery at the community level."

### **SARS-CoV-2 Virus and Variants**

### News in Brief

"How do people resist COVID infections? Hospital workers offer a hint — Immune cells might 'abort' SARS-CoV-2 infection, forestalling a positive PCR or antibody test" (Nature).

"Do childhood colds help the body respond to COVID? A mechanism known as 'original antigenic sin' protects some people from flu; whether it helps immune reactions to coronaviruses is still unclear" (Nature).

"Dissecting the early COVID-19 cases in Wuhan" (Science).

"New coronavirus, likely from dogs, infects people in Malaysia and Haiti" (NPR).

Speaking of Animals...

"Infection with SARS-CoV-2 variant B.1.1.7 detected in a group of dogs and cats with suspected myocarditis" (<u>Vet Rec</u>).

"Three snow leopards die of COVID-19 at Nebraska zoo" (CBS).

"Denver Zoo reports world's first coronavirus cases in hyenas" (AP).

#### Journal Articles

Emerg Infect Dis: <u>Multistate Outbreak of SARS-CoV-2 Infections, Including Vaccine</u>

<u>Breakthrough Infections, Associated with Large Public Gatherings, United States</u> (18 November 2021)

"During July 2021, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) B.1.617.2 variant infections, including vaccine breakthrough infections, occurred after large public gatherings in Provincetown, Massachusetts, USA, prompting a multistate investigation. Public health departments identified primary and secondary cases by using coronavirus disease surveillance data, case investigations, and contact tracing. A primary case was defined as SARS-CoV-2 detected <14 days after travel to or residence in Provincetown during July 3-17. A secondary case was defined as SARS-CoV-2 detected <14 days after close contact with a person who had a primary case but without travel to or residence in Provincetown during July 3-August 10. We identified 1,098 primary cases and 30 secondary cases associated with 26 primary cases among fully and non-fully vaccinated persons. Large gatherings can have widespread effects on SARS-CoV-2 transmission, and fully vaccinated persons should take precautions, such as masking, to prevent SARS-CoV-2 transmission, particularly during substantial or high transmission."

Clin Microbiol Infect: Rectally shed SARS-CoV-2 in COVID-19 inpatients is consistently lower than respiratory shedding and lacks infectivity (09 November 2021)

"Objectives: Assessment of whether SARS-CoV-2 has been propagated during intestinal passage and infectivity is conserved when shed rectally by hospitalised patients.

Methods: An exploratory cohort study including 28 COVID-19 inpatients with estimation of RNA levels by RT-PCR and viral infectivity by culturing of viral material sampled concomitantly and identically from pharynx and rectum.

Results: SARS-CoV-2 RNA was detected more frequently (91%, 30/33 vs. 42%, 14/33, p<0.0001) and at higher concentrations (median levels 2,190,186 IU/mL vs. 13,014 IU/mL, p<0.0001) in the pharyngeal swabs than in the rectal swabs. For all sample pairs (n=33) the rectal swabs contained undetectable or lower SARS-CoV-2 RNA concentrations than their paired pharyngeal swabs. Replicative virus was found in 37% (11/30) of the PCR-positive pharyngeal swabs, whereas none of the PCR-positive rectal swabs could be cultured (0%, 0/14) despite containing SARS-CoV-2 RNA concentrations up to 1,544,691 IU/mL.

Conclusions: Our data draw into question whether SARS-CoV-2 is transmitted readily from faeces."

Nat Commun: <u>A novel SARS-CoV-2 related coronavirus in bats from Cambodia</u> (09 November 2021)

"Knowledge of the origin and reservoir of the coronavirus responsible for the ongoing COVID-19 pandemic is still fragmentary. To date, the closest relatives to SARS-CoV-2 have been detected in *Rhinolophus* bats sampled in the Yunnan province, China. Here we describe the identification of SARS-CoV-2 related coronaviruses in two *Rhinolophus shameli* bats sampled in Cambodia in 2010. Metagenomic sequencing identifies nearly identical viruses sharing 92.6% nucleotide identity with SARS-CoV-2. Most genomic regions are closely related to SARS-CoV-2, with the exception of a region of the spike, which is not compatible with human ACE2-mediated entry. The discovery of these viruses in a bat species not found in China indicates that SARS-CoV-2 related viruses have a much wider geographic distribution than previously reported, and suggests that Southeast Asia represents a key area to consider for future surveillance for coronaviruses."

Clin Infect Dis: <u>Symptoms and SARS-CoV-2 positivity in the general population in the UK</u> (08 November 2021)

"Background: 'Classic' symptoms (cough, fever, loss of taste/smell) prompt SARS-CoV-2 PCR-testing in the UK. Studies have assessed the ability of different symptoms to identify infection, but few have compared symptoms over time (reflecting variants) and by vaccination status.

Methods: Using the COVID-19 Infection Survey, sampling households across the UK, we compared symptoms in PCR-positives vs. PCR-negatives, evaluating sensitivity of combinations of 12 symptoms (percentage symptomatic PCR-positives reporting specific symptoms) and tests per case (TPC) (PCR-positives or PCR-negatives reporting specific symptoms/ PCR-positives reporting specific symptoms).

Results: Between April 2020 and August 2021, 27,869 SARS-CoV-2 PCR-positive episodes occurred in 27,692 participants (median 42 years), of whom 13,427 (48%) self-reported symptoms ("symptomatic PCR-positives"). The comparator comprised 3,806,692 test-negative visits (457,215 participants); 130,612 (3%) self-reported symptoms ("symptomatic PCR-negatives"). Symptom reporting in PCR-positives varied by age, sex, and ethnicity, and over time, reflecting changes in prevalence of viral variants, incidental changes (e.g. seasonal pathogens (with sore throat increasing in PCR-positives and PCR-negatives from April 2021), schools re-opening) and vaccination roll-out. After May-2021 when Delta emerged, headache and fever substantially increased in PCR-positives, but not PCR-negatives. Sensitivity of symptom-based detection increased from 74% using 'classic' symptoms, to 81% adding fatigue/weakness, and 90% including all eight additional symptoms. However, this increased TPC from 4.6 to 5.3 to 8.7.

Conclusions: Expanded symptom combinations may provide modest benefits for sensitivity of PCR-based case detection, but this will vary between settings and over time, and increases tests/case. Large-scale changes to targeted PCR-testing approaches require careful evaluation given substantial resource and infrastructure implications."

## **COVID-19 Vaccines**

### News in Brief

On Friday, 19 November 2021, the FDA authorized coronavirus boosters for people 18 and older who had previously received mRNA vaccine (i.e., Pfizer or Moderna) at least 6 months prior (FDA).

"How protein-based COVID vaccines could change the pandemic" (Nature).

A German advisory committee recommended that people under 30 should only receive the Pfizer/BioNTech vaccine because it of the lower risk of myocarditis (Reuters).

"Many Latin American travelers shut out from visiting U.S. by new vaccine policy — From Guatemala to Mexico to Cuba, millions of people have been vaccinated with shots not approved by the WHO, making them ineligible to enter the U.S." (NBC).

### Special Reports and Other Resources

NADEM: <u>Vaccine Research and Development to Advance Pandemic and Seasonal Influenza</u>
<u>Preparedness and Response: Lessons from COVID-19</u> (17 November 2021)

"The global response to COVID-19 has demonstrated the importance of vigilance and preparedness for infectious diseases, particularly influenza. There is a need for more effective influenza vaccines and modern manufacturing technologies that are adaptable and scalable to meet demand during a pandemic. The rapid development of COVID-19 vaccines has demonstrated what is possible with extensive data sharing, researchers who have the necessary resources and novel technologies to conduct and apply their research, rolling review by regulators, and public-private partnerships. As demonstrated throughout the response to COVID-19, the process of research and development of novel vaccines can be significantly optimized when stakeholders are provided with the resources and technologies needed to support their response.

Vaccine Research and Development to Advance Pandemic and Seasonal Influenza Preparedness and Response focuses on how to leverage the knowledge gained from the COVID-19 pandemic to optimize vaccine research and development (R&D) to support the prevention and control of seasonal and pandemic influenza. The committee's findings address four dimensions of vaccine R&D: (1) basic and translational science, (2) clinical science, (3) manufacturing science, and (4) regulatory science."

#### Journal Articles

MMWR: Incidence of SARS-CoV-2 Infection, Emergency Department Visits, and Hospitalizations
Because of COVID-19 Among Persons Aged ≥12 Years, by COVID-19 Vaccination Status —
Oregon and Washington, July 4—September 25, 2021 (19 November 2021)

"What is already known about this topic? Studies have demonstrated that SARS-CoV-2 infection, need for emergency department (ED) visits, and hospitalization were uncommon in fully vaccinated persons before the widespread circulation of the SARS-CoV-2 B.1.617.2 (Delta) variant.

What is added by this report? Among persons aged ≥12 years enrolled in a Pacific Northwest health plan, unvaccinated persons with SARS-CoV-2 infection were approximately twice as likely to receive ED care or to be hospitalized than were vaccinated persons with COVID-19.

What are the implications for public health practice? The findings in this report support CDC's current recommendation that all persons aged ≥5 years should receive full COVID-19

vaccination, including additional and booster doses, to prevent illness and reduce transmission of SARS-CoV-2."

Lancet: <u>Promoting COVID-19 vaccine acceptance: recommendations from the Lancet</u>

<u>Commission on Vaccine Refusal, Acceptance, and Demand in the USA</u> (15 November 2021)

"Since the first case of COVID-19 was identified in the USA in January, 2020, over 46 million people in the country have tested positive for SARS-CoV-2 infection. Several COVID-19 vaccines have received emergency use authorisations from the US Food and Drug Administration, with the Pfizer–BioNTech vaccine receiving full approval on Aug 23, 2021. When paired with masking, physical distancing, and ventilation, COVID-19 vaccines are the best intervention to sustainably control the pandemic. However, surveys have consistently found that a sizeable minority of US residents do not plan to get a COVID-19 vaccine. The most severe consequence of an inadequate uptake of COVID-19 vaccines has been sustained community transmission (including of the delta [B.1.617.2] variant, a surge of which began in July, 2021). Exacerbating the direct impact of the virus, a low uptake of COVID-19 vaccines will prolong the social and economic repercussions of the pandemic on families and communities, especially low-income and minority ethnic groups, into 2022, or even longer. The scale and challenges of the COVID-19 vaccination campaign are unprecedented. Therefore, through a series of recommendations, we present a coordinated, evidence-based education, communication, and behavioural intervention strategy that is likely to improve the success of COVID-19 vaccine programmes across the USA."

MMWR: <u>The Advisory Committee on Immunization Practices' Interim Recommendation for Use of Pfizer-BioNTech COVID-19 Vaccine in Children Aged 5–11 Years — United States, November 2021</u> (12 November 2021)

"What is already known about this topic? On October 29, 2021, the Food and Drug Administration granted Emergency Use Authorization for the Pfizer-BioNTech COVID-19 vaccine for children aged 5–11 years.

What is added by this report? On November 2, 2021, after a systematic review of available data, the Advisory Committee on Immunization Practices made an interim recommendation for use of the Pfizer-BioNTech COVID-19 vaccine in children aged 5–11 years in the United States for prevention of COVID-19.

What are the implications for public health practice? The Pfizer-BioNTech COVID-19 vaccine has high efficacy (>90%) against COVID-19 in children aged 5–11 years, and benefits outweigh risks for vaccination. Vaccination is important to protect children against COVID-19 and reduce community transmission of SARS-CoV-2."

Clin Infect Dis: <u>Myocarditis Following COVID-19 mRNA Vaccine: A Case Series and Incidence</u>
<u>Rate Determination</u> (03 November 2021)

"Background: Myocarditis following COVID-19 mRNA vaccines (Pfizer-BioNTech and Moderna) have been increasingly reported. Incidence rates in the general population are lacking, with pericarditis rather than myocarditis diagnostic codes being used to estimate background rates. This comparison is critical to balance the risk of vaccination with the risk of no vaccination.

Methods: A retrospective case-series was performed utilizing the Mayo Clinic COVID-19 Vaccine Registry. We measured the incidence rate ratio for myocarditis temporally related to COVID-19 mRNA vaccination compared to myocarditis in a comparable population from 2016 through 2020. Clinical characteristics and outcomes of the affected patients was collected. A total of 21 individuals were identified, but ultimately 7 patients met the inclusion criteria for vaccine-associated myocarditis.

Results: The overall incidence rate ratio (IRR) of COVID-19 related myocarditis was 4.18 (CI95% 1.63, 8.98) which was entirely attributable to an increased IRR among adult males (IRR 6.69, CI95% 2.35, 15.52) compared to females (IRR 1.41, CI95% 0.03, 8.45). All cases occurred within 2 weeks of a dose of the COVID-19 mRNA vaccine with the majority occurring within 3 days (range 1-13 days) following the second dose (6/7 patients, 86%). Overall, cases were mild, and all patients survived.

Conclusions: Myocarditis is a rare adverse event associated with COVID-19 mRNA vaccines, and in adult males it occurs with significantly higher incidence than the background population rate. Recurrence of myocarditis after a subsequent mRNA vaccine dose is not known at this time."

### **Breakthrough Infections, Reinfections, and Coinfections**

### News in Brief

"The double-whammy COVID-flu — It's becoming clear that 'coinfections' happen all the time. Just how bad are they?" (Atlantic).

"How easily can vaccinated people spread COVID? Vaccination is the best protection against infection. But when breakthroughs do occur, a very basic question still has an unsatisfying answer" (Atlantic).

### Journal Articles

J Infect Dis: <u>Monoclonal Antibody Treatment of Breakthrough COVID-19 in Fully Vaccinated Individuals with High-Risk Comorbidities</u> (16 November 2021)

"Breakthrough COVID-19 may occur in fully vaccinated persons. In this cohort of 1395 persons (mean age, 54.3 years; 60% female; median body mass index, 30.7) who developed breakthrough COVID-19, there were 107 (7.7%) who required hospitalization by day 28. Hospitalization was significantly associated with the number of medical comorbidities. Antispike monoclonal antibody treatment was significantly associated with a lower risk of hospitalization (Odds Ratio: 0.227; 95% confidence interval, 0.128 - 0.403; p<0.001). The number needed to treat (NNT) to prevent one hospitalization was 225 among the lowest-risk patient group compared to NNT of 4 among those with highest numbers of medical comorbidity."

Clin Infect Dis: Reinfection with SARS-CoV-2 among previously infected healthcare personnel and first responders (15 November 2021)

"Background: SARS-CoV-2 virus testing among first responders and healthcare personnel who participated in a May-August 2020 serosurvey which assessed spike protein antibodies (S1 region) provided an opportunity to assess reinfection.

Methods: Serology survey data were merged with virus testing results from Rhode Island (March 1, 2020-February 17, 2021) and New York City (March 10-December 14, 2020). Participants with a positive virus test ≥14 days before their serology test were included. Reinfection was defined as a second positive SARS-CoV-2 test result ≥90 days after the first positive test. The association between serostatus and reinfection was assessed with a proportional hazards model adjusting for demographics, exposures, and virus testing frequency.

Results: Among 1,572 previously infected persons, 40 (2.5%) were reinfected. Reinfection differed by serostatus: 8.4% among seronegative versus 1.9% among seropositive participants (p<0.0001). Most reinfections occurred among Rhode Island nursing home and corrections (RINHC) personnel (n=30) who were most frequently tested (mean 30.3 tests versus 4.6 for other Rhode Island and 2.3 for New York City participants). The adjusted hazard ratio (aHR) for reinfection in seropositive versus seronegative persons was 0.41 (95% CI 0.20, 0.81). Exposure to a household member with COVID-19 before the serosurvey was also protective (aHR 0.34, 95% CI 0.13, 0.89).

Conclusions: Reinfections were uncommon among previously infected persons over a 9-month period that preceded widespread variant circulation. Seropositivity decreased reinfection risk. Lower reinfection risk associated with exposure to a household member

with COVID-19 before the serosurvey may reflect subsequently reduced household transmission among members of previously infected households."

Clin Infect Dis: <u>SARS-CoV-2 reinfection associates with unstable housing and occurs in the presence of antibodies</u> (10 November 2021)

"Background: The factors associated with severe acute respiratory coronavirus 2 (SARS-CoV-2) reinfection remain poorly defined.

Methods: We identified patients with SARS-CoV-2 infection and at least one repeat reverse transcription (RT) - polymerase chain reaction (PCR) result a minimum of 90 days after the initial positive test and prior to January 21, 2021. Those with a repeat positive test were deemed to have reinfection (n = 75), and those with only negative tests were classified as convalescents (n = 1,594). Demographics, coronavirus disease 2019 (COVID-19) severity, and treatment histories were obtained from the Boston Medical Center electronic medical record. Humoral responses were analyzed using SARS-CoV-2 specific enzyme linked immunosorbent assays and pseudovirus neutralizations in subset of reinfection (n = 16) and convalescent samples (n = 32). Univariate, multivariate, and time to event analyses were used to identify associations.

Results: Individuals with reinfection had more frequent testing at shorter intervals compared to the convalescents. Unstable housing was associated with more than two-fold greater chance of reinfection. Pre-existing comorbidities and COVID-19 severity after the initial infection were not associated with reinfection. SARS-CoV-2 IgG levels and pseudovirus neutralization were not different within the early weeks after primary infection and at a time-point at least 90 days later in the two groups. In the convalescents, but not in those with reinfection, the late as compared to early humoral responses were significantly higher.

Conclusions: Reinfection associates with unstable housing, which is likely a marker for virus exposure, and reinfection occurs in the presence of SARS-CoV-2 antibodies."

### **Treatments and Management**

#### News in Brief

"For at least eight months following a single dose, the REGEN-COV COVID-19 drug cocktail developed by Regeneron Pharmaceuticals, Inc. could provide affiliated risk reductions of 81.6 percent, according to a new analysis of a Phrase 3 trial" (HPN; see also: Regeneron news release).

"AstraZeneca announced that its antibody cocktail reduced the risk of developing symptomatic COVID-19 by 83% over 6 months in a prevention trial and reduced the risk of developing severe symptoms by 88% when taken within 3 days of symptom onset in a treatment trial" (Medpage; see also: AstraZeneca new release).

## COVID pills

"Pfizer submits FDA application for emergency approval of Covid treatment pill" (CNBC).

"Pfizer to allow generic versions of its COVID pill in 95 countries" (Reuters).

"8 lingering questions about the new Covid pills from Merck and Pfizer" (STAT).

"COVID antiviral pills: what scientists still want to know — Drugs such as molnupiravir and Paxlovid could change the course of the pandemic if clinical trial results hold up in the real world" (Nature).

#### Journal Articles

Clin Infect Dis: Efficacy of Early Treatment with Favipiravir on Disease Progression among High Risk COVID-19 Patients: A Randomized, Open-Label Clinical Trial (19 November 2021)

"Background: Role of favipiravir in preventing disease progression in COVID-19 remains uncertain. We aimed to determine its effect in preventing disease progression from non-hypoxia to hypoxia among high risk COVID-19 patients.

Study design: This was an open-label, randomized clinical trial conducted at 14 public hospitals across Malaysia from February to June 2021 among 500 symptomatic, RT-PCR confirmed COVID-19 patients, aged ≥50 years with ≥1 co-morbidity, and hospitalized within first 7 days of illness. Patients were randomized on 1:1 ratio to favipiravir plus standard care or standard care alone. Favipiravir was administered at 1800mg twice-daily on day 1 followed by 800mg twice-daily until day 5. The primary endpoint was rate of clinical progression from non-hypoxia to hypoxia. Secondary outcomes included rates of mechanical ventilation, intensive care unit (ICU) admission, and in-hospital mortality.

Results: Among 500 patients randomized (mean age, 62.5 [SD 8.0] years; 258 women [51.6%]; and 251 [50.2%] had COVID-19 pneumonia), 487 (97.4%) completed the trial. Clinical progression to hypoxia occurred in 46 (18.4%) patients on favipiravir plus standard care and 37 (14.8%) on standard care alone (OR 1.30; 95%CI, 0.81-2.09; P=.28). All three pre-specified secondary end points were similar between both groups. Mechanical ventilation occurred in 6 (2.4%) vs 5 (2.0%) (OR 1.20; 95%CI, 0.36-4.23; P=.76), ICU admission in 13 (5.2%) vs 12 (4.8%) (OR 1.09; 95%CI, 0.48-2.47; P=.84), and in-hospital mortality in 5 (2.0%) vs 0 (OR 12.54; 95%CI, 0.76- 207.84; P=.08).

Conclusions: Among COVID-19 patients at high risk of disease progression, early treatment with oral favipiravir did not prevent their disease progression from non-hypoxia to hypoxia."

Lancet: <u>Aspirin in patients admitted to hospital with COVID-19 (RECOVERY): a randomised, controlled, open-label, platform trial (17 November 2021)</u>

"Background: Aspirin has been proposed as a treatment for COVID-19 on the basis of its anti-thrombotic properties. We aimed to evaluate the efficacy and safety of aspirin in patients admitted to hospital with COVID-19.

Methods: In this randomised, controlled, open-label, platform trial, several possible treatments were compared with usual care in patients hospitalised with COVID-19. The trial took place at 177 hospitals in the UK, two hospitals in Indonesia, and two hospitals in Nepal. Eligible and consenting adults were randomly allocated in a 1:1 ratio to either usual standard of care plus 150 mg aspirin once per day until discharge or usual standard of care alone using web-based simple (unstratified) randomisation with allocation concealment. The primary outcome was 28 day mortality. All analyses were done by intention to treat. The trial is registered with ISRCTN (50189673) and ClinicalTrials.gov (NCT04381936).

Findings: Between Nov 1, 2020, and March 21, 2021, 14 892 (66%) of 22 560 patients enrolled into the RECOVERY trial were eligible to be randomly allocated to aspirin. 7351 patients were randomly allocated (1:1) to receive aspirin and 7541 patients to receive usual care alone. Overall, 1222 (17%) of 7351 patients allocated to aspirin and 1299 (17%) of 7541 patients allocated to usual care died within 28 days (rate ratio 0.96, 95% CI 0.89-1.04; p=0.35). Consistent results were seen in all prespecified subgroups of patients. Patients allocated to aspirin had a slightly shorter duration of hospitalisation (median 8 days, IQR 5 to >28, vs 9 days, IQR 5 to >28) and a higher proportion were discharged from hospital alive within 28 days (75% vs 74%; rate ratio 1.06, 95% CI 1.02-1.10; p=0.0062). Among patients not on invasive mechanical ventilation at baseline, there was no significant difference in the proportion meeting the composite endpoint of invasive mechanical ventilation or death (21% vs 22%; risk ratio 0.96, 95% CI 0.90-1.03; p=0.23). Aspirin use was associated with a reduction in thrombotic events (4.6% vs 5.3%; absolute reduction 0.6%, SE 0.4%) and an increase in major bleeding events (1.6% vs 1.0%; absolute increase 0.6%, SE 0.2%).

Interpretation: In patients hospitalised with COVID-19, aspirin was not associated with reductions in 28 day mortality or in the risk of progressing to invasive mechanical ventilation or death, but was associated with a small increase in the rate of being discharged alive within 28 days."

Ann Intern Med: <u>Comparative Effectiveness of an Automated Text Messaging Service for</u> Monitoring COVID-19 at Home (16 November 2021)

"Background: Although most patients with SARS-CoV-2 infection can be safely managed at home, the need for hospitalization can arise suddenly.

Objective: To determine whether enrollment in an automated remote monitoring service for community-dwelling adults with COVID-19 at home ("COVID Watch") was associated with improved mortality.

Design: Retrospective cohort analysis.

Setting: Mid-Atlantic academic health system in the United States.

Participants: Outpatients who tested positive for SARS-CoV-2 between 23 March and 30 November 2020.

Intervention: The COVID Watch service consists of twice-daily, automated text message check-ins with an option to report worsening symptoms at any time. All escalations were managed 24 hours a day, 7 days a week by dedicated telemedicine clinicians.

Measurements: Thirty- and 60-day outcomes of patients enrolled in COVID Watch were compared with those of patients who were eligible to enroll but received usual care. The primary outcome was death at 30 days. Secondary outcomes included emergency department (ED) visits and hospitalizations. Treatment effects were estimated with propensity score-weighted risk adjustment models.

Results: A total of 3488 patients enrolled in COVID Watch and 4377 usual care control participants were compared with propensity score weighted models. At 30 days, COVID Watch patients had an odds ratio for death of 0.32 (95% CI, 0.12 to 0.72), with 1.8 fewer deaths per 1000 patients (CI, 0.5 to 3.1) (P = 0.005); at 60 days, the difference was 2.5 fewer deaths per 1000 patients (CI, 0.9 to 4.0) (P = 0.002). Patients in COVID Watch had more telemedicine encounters, ED visits, and hospitalizations and presented to the ED sooner (mean, 1.9 days sooner [CI, 0.9 to 2.9 days]; all P < 0.001).

Limitation: Observational study with the potential for unobserved confounding.

Conclusion: Enrollment of outpatients with COVID-19 in an automated remote monitoring service was associated with reduced mortality, potentially explained by more frequent telemedicine encounters and more frequent and earlier presentation to the ED."

JAMA Netw Open: <u>Mortality Risk Among Patients With COVID-19 Prescribed Selective Serotonin</u>
<u>Reuptake Inhibitor Antidepressants</u> (15 November 2021)

"Question: Are selective serotonin reuptake inhibitors (SSRIs), specifically fluoxetine hydrochloride, associated with a lower mortality risk among patients with COVID-19?

Findings: In this multicenter cohort study analyzing electronic health records of 83 584 patients diagnosed with COVID-19, including 3401 patients who were prescribed SSRIs, a reduced relative risk of mortality was found to be associated with the use of SSRIs—specifically fluoxetine—compared with patients who were not prescribed SSRIs.

Meaning: These findings suggest that SSRI use may reduce mortality among patients with COVID-19, although they may be subject to unaccounted confounding variables; further investigation via large, randomized clinical trials is needed."

Clin Infect Dis: <u>Broad impacts of COVID-19 pandemic on acute respiratory infections in China:</u> an observational study (12 November 2021)

"Background: To combat the COVID-19 pandemic, nonpharmaceutical interventions (NPI) were implemented worldwide, which impacted a broad spectrum of acute respiratory infections (ARI).

Methods: Etiologically diagnostic data from 142 559 cases with ARIs, who were tested for eight viral pathogens (influenza virus, IFV; respiratory syncytial virus, RSV; human parainfluenza virus, HPIV; human adenovirus; human metapneumovirus; human coronavirus, HCoV; human bocavirus, HBoV, and human rhinovirus, HRV) between 2012 and 2021, were analyzed to assess the changes of respiratory infections in China during the first COVID-19 pandemic year compared to pre-pandemic years.

Results: Test positive rates of all respiratory viruses decreased during 2020, compared to the average levels during 2012–2019, with changes ranging from -17·2% for RSV to -87·6% for IFV. Sharp decreases mostly occurred between February and August when massive NPIs remained active, although HRV rebounded to the historical level during the summer. While IFV and HMPV were consistently suppressed year round, RSV, HPIV, HCoV, HRV HBoV resurged and went beyond historical levels during September, 2020–January, 2021, after NPIs were largely relaxed and schools reopened. Resurgence was more prominent among children younger than 18 years and in Northern China. These observations remain valid after accounting for seasonality and long-term trend of each virus.

Conclusions: Activities of respiratory viral infections were reduced substantially in the early phases of the COVID-19 pandemic, and massive NPIs were likely the main driver. Lifting of NPIs can lead to resurgence of viral infections, particularly in children."

### Pre-Existing Conditions, Comorbidities, and Impact on Other Health Issues

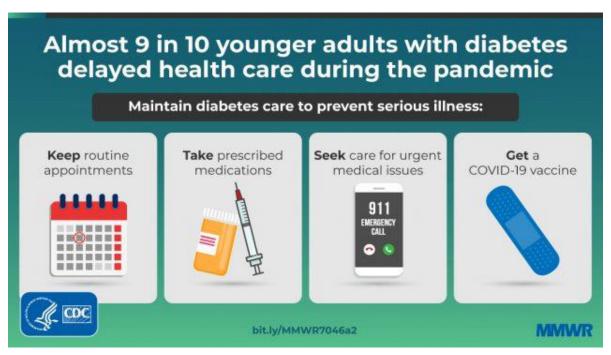
#### Journal Articles

MMWR: <u>Health Care Access and Use Among Adults with Diabetes During the COVID-19</u> Pandemic — United States, February—March 2021 (19 November 2021)

"What is already known about this topic? Persons with diabetes are at high risk for severe COVID-19, and the COVID-19 pandemic has affected diabetes care and management in the United States.

What is added by this report? Among adults with diabetes, those aged 18–29 years reported the most disruption in access to and use of medical care and the least engagement in prevention of COVID-19, including vaccination intent.

What are the implications for public health practice? Efforts are warranted to enhance access to diabetes care during the COVID-19 pandemic, and to deliver public health messages emphasizing the importance of diabetes management and COVID-19 prevention, including vaccination, especially among younger adults with diabetes."



JAMA Oncol: <u>SARS-CoV-2 Spike-Specific T-Cell Responses in Patients With B-Cell Depletion Who</u> Received Chimeric Antigen Receptor T-Cell Treatments (18 November 2021)

"This cohort study examines the ability of patients receiving chimeric antigen receptor T-cell treatments to mount T-cell immunity in response to messenger RNA vaccines for severe acute respiratory syndrome coronavirus 2 despite substantial B-cell depletion....

Although this study is limited by its small sample size, we show that immune responses to SARS-CoV-2 mRNA vaccines are induced for the majority of patients who have been treated with CAR T-cell therapies targeting B-cell lineage antigens. An induction of a vaccine-specific antibody was associated with the level of circulating B cells. However, strong CD4 T-cell responses were observed even for some patients with severe humoral immune deficiency. Further refinement of vaccination strategies to promote cell-mediated immunity may enhance immune protection for individuals with B-cell deficiency."

Lancet Rheumatol: <u>Long-term use of immunosuppressive medicines and in-hospital COVID-19</u> <u>outcomes: a retrospective cohort study using data from the National COVID Cohort</u> <u>Collaborative</u> (15 November 2021)

"Background: Many individuals take long-term immunosuppressive medications. We evaluated whether these individuals have worse outcomes when hospitalised with COVID-19 compared with non-immunosuppressed individuals.

Methods: We conducted a retrospective cohort study using data from the National COVID Cohort Collaborative (N3C), the largest longitudinal electronic health record repository of patients in hospital with confirmed or suspected COVID-19 in the USA, between Jan 1, 2020, and June 11, 2021, within 42 health systems. We compared adults with immunosuppressive medications used before admission to adults without long-term immunosuppression. We considered immunosuppression overall, as well as by 15 classes of medication and three broad indications for immunosuppressive medicines. We used Fine and Gray's proportional subdistribution hazards models to estimate the hazard ratio (HR) for the risk of invasive mechanical ventilation, with the competing risk of death. We used Cox proportional hazards models to estimate HRs for in-hospital death. Models were adjusted using doubly robust propensity score methodology.

Findings: Among 231 830 potentially eligible adults in the N3C repository who were admitted to hospital with confirmed or suspected COVID-19 during the study period, 222 575 met the inclusion criteria (mean age 59 years [SD 19]; 111 269 [50%] male). The most common comorbidities were diabetes (23%), pulmonary disease (17%), and renal disease (13%). 16 494 (7%) patients had long-term immunosuppression with medications for diverse conditions, including rheumatological disease (33%), solid organ transplant (26%), or cancer (22%). In the propensity score matched cohort (including 12 841 immunosuppressed patients and 29 386 non-immunosuppressed patients), immunosuppression was associated with a reduced risk of invasive ventilation (HR 0·89, 95% CI 0·83–0·96) and there was no overall association between long-term immunosuppression and the risk of in-hospital death. None of the 15 medication classes examined were associated with an increased risk of invasive mechanical ventilation. Although there was no statistically significant association between most drugs and inhospital death, increases were found with rituximab for rheumatological disease (1·72,

 $1\cdot10-2\cdot69$ ) and for cancer ( $2\cdot57$ ,  $1\cdot86-3\cdot56$ ). Results were generally consistent across subgroup analyses that considered race and ethnicity or sex, as well as across sensitivity analyses that varied exposure, covariate, and outcome definitions.

Interpretation: Among this cohort, with the exception of rituximab, there was no increased risk of mechanical ventilation or in-hospital death for the rheumatological, antineoplastic, or antimetabolite therapies examined."

JAMA Netw Open: <u>Association Between Androgen Deprivation Therapy and Mortality Among Patients With Prostate Cancer and COVID-19</u> (12 November 2021)

"Question: Given the higher COVID-19—related mortality rate observed among men than among women, is androgen deprivation therapy associated with decreased rate of 30-day mortality from COVID-19 among patients with prostate cancer?

Findings: In this cohort study of 1106 patients, no statistically significant difference was found in the rates of all cause 30-day mortality following COVID-19 infection among men with prostate cancer receiving androgen deprivation therapy (15%) vs those not receiving androgen deprivation therapy (14%).

Meaning: The findings of this cohort study do not support an association between androgen deprivation therapy and 30-day mortality among patients with COVID-19 infection."

JAMA Netw Open: <u>Association of Sleep-Related Hypoxia With Risk of COVID-19 Hospitalizations</u> and Mortality in a Large Integrated Health System (10 November 2021)

"Question: Are sleep-disordered breathing and sleep-related hypoxia associated with SARS-CoV-2 infection and COVID-19 outcomes?

Findings: In this case-control study of 5402 patients in a large integrated health system, sleep-disordered breathing and sleep-related hypoxia were not associated with an increased likelihood of contracting SARS-CoV-2. After accounting for confounding factors including cardiopulmonary disease, cancer, and smoking exposure, sleep-related hypoxia indices were associated with more severe COVID-19 clinical outcomes, including hospitalization and mortality, in time-to-event analyses.

Meaning: These results suggest that baseline sleep-related hypoxia may portend worse clinical prognosis in COVID-19."

J Clin Oncol: <u>Immunogenicity and Reactogenicity of SARS-CoV-2 Vaccines in Patients With</u> Cancer: The CANVAX Cohort Study (09 November 2021)

"Purpose: The immunogenicity and reactogenicity of SARS-CoV-2 vaccines in patients with cancer are poorly understood.

Methods: We performed a prospective cohort study of adults with solid-organ or hematologic cancers to evaluate anti-SARS-CoV-2 immunoglobulin A/M/G spike antibodies, neutralization, and reactogenicity ≥ 7 days following two doses of mRNA-1273, BNT162b2, or one dose of Ad26.COV2.S. We analyzed responses by multivariate regression and included data from 1,638 healthy controls, previously reported, for comparison.

Results: Between April and July 2021, we enrolled 1,001 patients; 762 were eligible for analysis (656 had neutralization measured). mRNA-1273 was the most immunogenic (log10 geometric mean concentration [GMC] 2.9, log10 geometric mean neutralization titer [GMT] 2.3), followed by BNT162b2 (GMC 2.4; GMT 1.9) and Ad26.COV2.S (GMC 1.5; GMT 1.4; P < .001). The proportion of low neutralization (< 20% of convalescent titers) among Ad26.COV2.S recipients was 69.9%. Prior COVID-19 infection (in 7.1% of the cohort) was associated with higher responses (P < .001). Antibody titers and neutralization were quantitatively lower in patients with cancer than in comparable healthy controls, regardless of vaccine type (P < .001). Receipt of chemotherapy in the prior year or current steroids were associated with lower antibody levels and immune checkpoint blockade with higher neutralization. Systemic reactogenicity varied by vaccine and correlated with immune responses (P = .002 for concentration, P = .016 for neutralization). In 32 patients who received an additional vaccine dose, side effects were similar to prior doses, and 30 of 32 demonstrated increased antibody titers (GMC 1.05 before additional dose, 3.17 after dose).

Conclusion: Immune responses to SARS-CoV-2 vaccines are modestly impaired in patients with cancer. These data suggest utility of antibody testing to identify patients for whom additional vaccine doses may be effective and appropriate, although larger prospective studies are needed."

### Long COVID / Post-COVID Period

### News in Brief

"Could long covid unlock clues to chronic fatigue and other poorly understood conditions?" (WP)

<sup>&</sup>quot;New clues to the biology of long COVID are starting to emerge" (NPR).

<sup>&</sup>quot;She died with long covid. Should her organs have been donated?" (NYT; requires login).

<sup>&</sup>quot;COVID can cause strange eye and ear symptoms — From conjunctivitis to vertigo, coronavirus infections can affect disparate senses" (Sci Am).

#### **Journal Articles**

JAMA Otolaryngol Head Neck Surg: <u>Growing Public Health Concern of COVID-19 Chronic Olfactory Dysfunction</u> (18 November 2021)

"This meta-analysis examines the scale of the public health concern of COVID-19—related chronic olfactory dysfunction...

This analysis of new daily cases of COVID-19, acute incidence of OD, and rates of recovery suggest that more than 700 000, and possibly as many as 1.6 million, US individuals experience COD because of SARS-CoV-2. To put this number in context, before the COVID-19 pandemic, the National Institute on Deafness and Other Communication Disorders estimated that, among US adults 40 years or older, measurable OD was found in up to 13.3 million adults. Notably, the age-specific prevalence of OD is 4.2% for individuals between age 40 to 49 years and 39.4% for individuals 80 years and older. The addition of 0.7 to 1.6 million new cases of COD represents a 5.3% to 12% relative increase. COVID-19 affects a younger demographic group than other causes of OD. Thus, the lifelong burden of OD will be much greater for the COVID-19 cohort than for patients in the older age groups. The true number of COD may be far higher than the results in this article indicate."

JAMA Intern Med: <u>Association of Self-reported COVID-19 Infection and SARS-CoV-2 Serology</u>
<u>Test Results With Persistent Physical Symptoms Among French Adults During the COVID-19</u>
Pandemic (08 November 2021)

"Question: Are the belief in having had COVID-19 infection and actually having had the infection as verified by SARS-CoV-2 serology testing associated with persistent physical symptoms during the COVID-19 pandemic?

Findings: In this cross-sectional analysis of 26 823 adults from the population-based French CONSTANCES cohort during the COVID-19 pandemic, self-reported COVID-19 infection was associated with most persistent physical symptoms, whereas laboratory-confirmed COVID-19 infection was associated only with anosmia. Those associations were independent from self-rated health or depressive symptoms.

Meaning: Findings suggest that persistent physical symptoms after COVID-19 infection should not be automatically ascribed to SARS-CoV-2; a complete medical evaluation may be needed to prevent erroneously attributing symptoms to the virus."

### Women's Health, Pregnancy, and Perinatal Care

### Journal Articles

MMWR: Risk for Stillbirth Among Women With and Without COVID-19 at Delivery Hospitalization — United States, March 2020–September 2021 (19 November 2021)

"What is already known about this topic? Pregnant women are at increased risk for severe disease from COVID-19, and COVID-19 is associated with an increased risk for adverse perinatal outcomes.

What is added by this report? Among 1,249,634 delivery hospitalizations during March 2020–September 2021, U.S. women with COVID-19 were at increased risk for stillbirth compared with women without COVID-19 (adjusted relative risk [aRR] = 1.90; 95% CI = 1.69–2.15). The magnitude of association was higher during the period of SARS-CoV-2 B.1.617.2 (Delta) variant predominance than during the pre-Delta period.

What are the implications for public health practice? Implementing evidence-based COVID-19 prevention strategies, including vaccination before or during pregnancy, is critical to reduce the impact of COVID-19 on stillbirths."

MMWR: <u>COVID-19</u>—<u>Associated Deaths After SARS-CoV-2 Infection During Pregnancy — Mississippi, March 1, 2020—October 6, 2021 (19 November 2021)</u>

"This report describes 15 COVID-19—associated deaths after infection with SARS-CoV-2 (the virus that causes COVID-19) during pregnancy in Mississippi during March 1, 2020—October 6, 2021....

This study found 15 COVID-19—associated deaths after SARS-CoV-2 infection during pregnancy (nine deaths per 1,000 SARS-CoV-2 infections); during the same period, 413 COVID-19—associated deaths were reported among females of reproductive age (2.5 deaths per 1,000 SARS-CoV-2 infections). In addition, this study found an apparent increase in the ratio of COVID-19—associated deaths per 1,000 cases among pregnant women as the Delta variant became predominant (pre-Delta period: five deaths per 1,000 SARS-CoV-2 infections during pregnancy; Delta predominance period: 25 deaths per 1,000 SARS-CoV-2 infections during pregnancy)."

Clin Infect Dis: <u>Universal SARS-CoV-2 testing for obstetric inpatient units across the United States</u> (17 November 2021)

"Background: The purpose of this study was to estimate prevalence of asymptomatic SARS-CoV-2 infection among patients admitted to obstetric inpatient units throughout the United States as detected by universal screening. We sought to describe the relationship between obstetric inpatient asymptomatic infection rates and publicly available surrounding community infection rates.

Methods: This was a cross-sectional study in which medical centers reported rates of positive SARS-CoV-2 testing in asymptomatic pregnant and immediate postpartum patients over a 1-3-month time span in 2020. Publicly reported SARS-CoV-2 case rates from the relevant county and state for each center were collected from the COVID Act Now dashboard and the COVID Tracking Project for correlation analysis.

Results: Data were collected from nine health centers, encompassing 18 hospitals. Participating health centers were located in Alabama, California, Illinois, Louisiana, New Jersey, North Carolina, Pennsylvania, Rhode Island, Utah, and Washington State. Each hospital had an active policy for universal SARS-CoV-2 testing on obstetric inpatient unit. A total of 10,147 SARS-CoV-2 tests were administered, of which 124 were positive (1.2%). Positivity rates varied by site, ranging from 0-3.2%. While SARS-CoV-2 infection rates were lower in asymptomatic obstetric inpatient groups than the surrounding communities, there was a positive correlation between positivity rates in obstetric inpatient units and their surrounding county (p=.003, r=.782) and state (p=.007, r=.708).

Conclusions: Given the correlation between community and obstetric inpatient rates, the necessity of SARS-CoV-2 related healthcare resource utilization in obstetric inpatient units may be best-informed by surrounding community infection rates."

JAMA Pediatr: <u>Association of Human Milk Antibody Induction, Persistence, and Neutralizing</u> Capacity With SARS-CoV-2 Infection vs mRNA Vaccination (10 November 2021)

"Question: How does human milk antibody composition and neutralization activity differ between lactating parents with COVID-19 infection vs those with COVID-19 messenger RNA vaccination?

Findings: In this cohort study of a convenience sample of 47 lactating parents with infection and 30 lactating parents who were vaccinated, antibody response in milk after infection was IgA dominant and highly variable while vaccination was associated with a robust IgG response, which began to decline by 90 days after the second vaccine dose. Milk from both groups showed neutralization activity against live SARS-CoV-2 virus, which can be attributed to IgA and IgG SARS-CoV-2 antibodies.

Meaning: COVID-19 infection and vaccination may result in significant antibodies in human milk that exhibit different temporal patterns, but both neutralize live SARS-CoV-2 virus."

### **Healthcare Workers**

### News in Brief

Long Reads

"Why health-care workers are quitting in droves: About one in five health-care workers has left medicine since the pandemic started. This is their story—and the story of those left behind" (Atlantic).

"Filipino American health workers reflect on trauma and healing on COVID's frontlines" (NPR).

#### **Journal Articles**

Am J Infect Control: <u>COVID-19 vaccination coverage among hospital-based healthcare</u> <u>personnel reported through the Department of Health and Human Services Unified Hospital</u> <u>Data Surveillance System, United States, January 20, 2021-September 15, 2021</u> (17 November 2021)

"To protect both patients and staff, healthcare personnel (HCP) were among the first groups in the United States recommended to receive the COVID-19 vaccine. We analyzed data reported to the U.S. Department of Health and Human Services (HHS) Unified Hospital Data Surveillance System on COVID-19 vaccination coverage among hospital-based HCP. After vaccine introduction in December 2020, COVID-19 vaccine coverage rose steadily through April 2021, but the rate of uptake has since slowed; as of September 15, 2021, among 3,357,348 HCP in 2,086 hospitals included in this analysis, 70.0% were fully vaccinated. Additional efforts are needed to improve COVID-19 vaccine coverage among HCP."

!!! NEW GUIDELINES Clin Infect Dis: Infectious Diseases Society of America Guidelines on Infection Prevention for Healthcare Personnel Caring for Patients with Suspected or Known COVID-19 (15 November 2021)

"Background: Since its emergence in late 2019, SARS-CoV-2 continues to pose a risk to healthcare personnel (HCP) and patients in healthcare settings. Although all clinical interactions likely carry some risk of transmission, human actions like coughing and care activities like aerosol-generating procedures likely have a higher risk of transmission. The rapid emergence and global spread of SARS-CoV-2 continues to create significant challenges in healthcare facilities, particularly with shortages of personal protective equipment (PPE) used by HCP. Evidence-based recommendations for what PPE to use in conventional, contingency, and crisis standards of care continue to be needed. Where evidence is lacking, the development of specific research questions can help direct funders and investigators.

Objective: Develop evidence-based rapid guidelines intended to support HCP in their decisions about infection prevention when caring for patients with suspected or known COVID-19.

Methods: IDSA formed a multidisciplinary guideline panel including frontline clinicians, infectious disease specialists, experts in infection control, and guideline methodologists with representation from the disciplines of public health, medical microbiology, pediatrics, critical care medicine and gastroenterology. The process followed a rapid recommendation checklist. The panel prioritized questions and outcomes. Then a systematic review of the peer-reviewed and grey literature was conducted. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to assess the certainty of evidence and make recommendations.

Results: The IDSA guideline panel agreed on eight recommendations, including two updated recommendations and one new recommendation added since the first version of the guideline. Narrative summaries of other interventions undergoing evaluations are also included.

Conclusions: Using a combination of direct and indirect evidence, the panel was able to provide recommendations for eight specific questions on the use of PPE for HCP providing care for patients with suspected or known COVID-19. Where evidence was lacking, attempts were made to provide potential avenues for investigation. There remain significant gaps in the understanding of the transmission dynamics of SARS-CoV-2 and PPE recommendations may need to be modified in response to new evidence. These recommendations should serve as a minimum for PPE use in healthcare facilities and do not preclude decisions based on local risk assessments or requirements of local health jurisdictions or other regulatory bodies."

## Mental Health, Psychosocial Issues, and Wellness

### News in Brief

"Thanksgiving means family, food — and plenty of harmful diet talk. Here's how to deal with it"  $(\underline{WP})$ .

### Journal Articles

Nature: Mental health concerns during the COVID-19 pandemic as revealed by helpline calls (17 November 2021)

"Mental health is an important component of public health, especially in times of crisis. However, monitoring public mental health is difficult because data are often patchy and low-frequency. Here we complement established approaches by using data from helplines, which offer a real-time measure of 'revealed' distress and mental health concerns across a range of topics. We collected data on 8 million calls from 19 countries, focusing on the COVID-19 crisis. Call volumes peaked six weeks after the initial outbreak, at 35% above prepandemic levels. The increase was driven mainly by fear (including fear of infection), loneliness and, later in the pandemic, concerns about physical health. Relationship issues, economic problems, violence and suicidal ideation, however, were less prevalent than before the pandemic. This pattern was apparent both during the first wave and during subsequent COVID-19 waves. Issues linked directly to the pandemic therefore seem to have replaced rather than exacerbated underlying anxieties. Conditional on infection rates, suicide-related calls increased when containment policies became more stringent and decreased when income support was extended. This implies that financial relief can allay the distress triggered by lockdown measures and illustrates the insights that can be gleaned from the statistical analysis of helpline data."

JAMA Netw Open: <u>Association of SARS-CoV-2 Infection With Psychological Distress,</u>

<u>Psychotropic Prescribing, Fatigue, and Sleep Problems Among UK Primary Care Patients</u> (17 November 2021)

"Question: Is SARS-CoV-2 infection associated with risk of subsequent psychiatric morbidity, sleep problems, or fatigue?

Findings: In this cohort study of the health care records of 11 923 105 patients, including 226 521 patients with SARS-CoV-2 infection, while infection was associated with increased risk of sleep problems and fatigue, associations with subsequent psychiatric morbidity were mixed.

Meaning: These findings suggest that psychiatric morbidity associated with SARS-CoV-2 infection may be overstated in analyses of health care records that do not sufficiently control for confounding."

JAMA Netw Open: <u>Trends in US Patients Receiving Care for Eating Disorders and Other Common Behavioral Health Conditions Before and During the COVID-19 Pandemic</u> (17 November 2021)

"This cohort study examines trends in care for eating disorders and other behavioral health conditions before and during the COVID-19 pandemic among commercially insured individuals in the US....

In this cohort study, we found that inpatient stays for eating disorders rose during the pandemic. Many aspects of the pandemic plausibly intensified eating disorders and their

ascertainment. The pandemic may have promoted disordered eating behaviors among susceptible individuals. For example, obesity was frequently cited as a risk factor for COVID severity; grocery shopping became more fraught in the early pandemic because of contagion concerns, new rules, and rituals; and many bought large quantities of foods to minimize shopping frequency or fear of shortage.4 Additionally, exercise may have become a focus of control or a compensatory mechanism for eating.6 Furthermore, the closing of schools and colleges may have helped families identify unhealthy eating or recognize its effects, and outpatient care may have been delayed until symptoms required hospitalization."

JAMA Netw Open: Experiences of Work-Family Conflict and Mental Health Symptoms by Gender Among Physician Parents During the COVID-19 Pandemic (12 November 2021)

"Question: Has the COVID-19 pandemic been associated with differences in careers and mental health between physician mothers and fathers?

Findings: In this cohort study of 276 physicians during the COVID-19 pandemic, mothers were more likely than fathers to be responsible for childcare or schooling and household tasks, to work primarily from home, to reduce their work hours, and to experience work-to-family conflict, family-to-work conflict, and depressive and anxiety symptoms. A gender difference in depressive symptoms was observed among physician parents during the COVID-19 pandemic that was not present before the pandemic.

Meaning: This study suggests that pandemic conditions are associated with an increase in gender inequalities within medicine and signals the importance of further attention and resources to mitigate the potential adverse consequences for the careers and well-being of physician mothers."

PLoS One: <u>Surviving SARS and living through COVID-19</u>: <u>Healthcare worker mental health outcomes and insights for coping</u> (10 November 2021)

"Objective: Explore how previous work during the 2003 Severe Acute Respiratory Syndrome (SARS) outbreak affects the psychological response of clinical and non-clinical healthcare workers (HCWs) to the current COVID-19 pandemic.

Methods: A cross-sectional, multi-centered hospital online survey of HCWs in the Greater Toronto Area, Canada. Mental health outcomes of HCWs who worked during the COVID-19 pandemic and the SARS outbreak were assessed using Impact of Events-Revised scale (IES-R), Generalized Anxiety Disorder scale (GAD-7), and Patient Health Questionnaire (PHQ-9).

Results: Among 3852 participants, moderate/severe scores for symptoms of post- traumatic stress disorder (PTSD) (50.2%), anxiety (24.6%), and depression (31.5%) were observed among HCWs. Work during the 2003 SARS outbreak was reported by 1116 respondents (29.1%), who had lower scores for symptoms of PTSD (P = .002), anxiety (P < .001), and

depression (P < .001) compared to those who had not worked during the SARS outbreak. Multivariable logistic regression analysis showed non-clinical HCWs during this pandemic were at higher risk of anxiety (OR, 1.68; 95% CI, 1.19-2.15, P = .01) and depressive symptoms (OR, 2.03; 95% CI, 1.34-3.07, P < .001). HCWs using sedatives (OR, 2.55; 95% CI, 1.61-4.03, P < .001), those who cared for only 2-5 patients with COVID-19 (OR, 1.59; 95% CI, 1.06-2.38, P = .01), and those who had been in isolation for COVID-19 (OR, 1.36; 95% CI, 0.96-1.93, P = .05), were at higher risk of moderate/severe symptoms of PTSD. In addition, deterioration in sleep was associated with symptoms of PTSD (OR, 4.68, 95% CI, 3.74-6.30, P < .001), anxiety (OR, 3.09, 95% CI, 2.11-4.53, P < .001), and depression (OR 5.07, 95% CI, 3.48-7.39, P < .001).

Conclusion: Psychological distress was observed in both clinical and non-clinical HCWs, with no impact from previous SARS work experience. As the pandemic continues, increasing psychological and team support may decrease the mental health impacts."

### **Disparities and Health Equity**

#### Journal Articles

JAMA Netw Open: <u>Disparities in COVID-19 Outcomes by Race, Ethnicity, and Socioeconomic</u> Status: A Systematic-Review and Meta-analysis (11 November 2021)

"Question: Are race and ethnicity—based COVID-19 outcome disparities in the United States associated with socioeconomic characteristics?

Findings: In this systematic review and meta-analysis of 4.3 million patients from 68 studies, African American, Hispanic, and Asian American individuals had a higher risk of COVID-19 positivity and ICU admission but lower mortality rates than White individuals. Socioeconomic disparity and clinical care quality were associated with COVID-19 mortality and incidence in racial and ethnic minority groups.

Meaning: In this study, members of racial and ethnic minority groups had higher rates of COVID-19 positivity and disease severity than White populations; these findings are important for informing public health decisions, particularly for individuals living in socioeconomically deprived communities."

BMJ Glob Health: <u>The influence of gender and ethnicity on facemasks and respiratory</u> protective equipment fit: a systematic review and meta-analysis (06 November 2021)

"Introduction: Black, Asian and minority ethnic (BAME) people are disproportionately affected by COVID-19. Respiratory protective equipment (RPE) has conventionally been

developed for a predominantly white male population that does not represent the healthcare workforce. The literature was reviewed to determine the protection offered to female and BAME users.

Methods: Five databases were searched. Eligible studies related to respirator fit in the context of anthropometrics, gender and ethnicity. Meta-analysis was performed for gender-based anthropometric differences. A priori protocol registration was not performed.

Results: 32 studies were included and anthropometric data was extracted from 15 studies. Meta-analysis revealed 14 anthropometric measurements were significantly smaller for females. Mean differences ranged from 0.37 mm to 22.05 mm. Gender-based anthropometric differences did not always translate to lower fit factor scores, with 12 studies reporting worse performance and fit for females and 10 reporting no gender effect. No studies provided disaggregate anthropometric data by ethnic group. Pass rates (PR) were low or moderate in 12 BAME or mixed-ethnicity cohorts. 14 studies reported associations between facial dimensions (FD) and respirator fit. Three comparative studies showed lower PR among selective BAME people. 18 studies reported RPE performance differed with model and design. Most studies did not prespecify inclusion/exclusion criteria. Small sample size and lack of justification or power calculations was a concern. Significant heterogeneity in study designs limited comparisons, particularly relating to respirator selection or availability and defining study outcomes relating to RPE performance.

Conclusion: The literature reports on largely Caucasian or single ethnic populations, and BAME people remain under-represented, limiting comparisons between ethnic groups. Facial anthropometrics vary between gender and likely between ethnicity, which may contribute to lower PR among females and ethnic minorities, particularly Asians. There is a need for studies including a broader spectrum of ethnicities and for consideration of female and BAME users during RPE development.

### Risk, Transmission, and Exposure

### News in Brief

"What would the public health experts do? STAT asked 28 about their holiday plans amid Covid-19" (STAT).

"Getting back to normal is only possible until you test positive. I was ultracareful for 18 months. Then I got COVID" (<u>Atlantic</u>).

"The upside of COVID hygiene theater. Yes, even at this stage of the pandemic" (Atlantic).



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Infographic: "How to Make Holiday Gatherings Safer: 6 Things to Keep in Mind" (Pandora Report).

#### **Journal Articles**

BMJ: Effectiveness of public health measures in reducing the incidence of covid-19, SARS-CoV-2 transmission, and covid-19 mortality: systematic review and meta-analysis (18 November 2021)

"Objective: To review the evidence on the effectiveness of public health measures in reducing the incidence of covid-19, SARS-CoV-2 transmission, and covid-19 mortality.

Design: Systematic review and metaanalysis.

Data sources: Medline, Embase, CINAHL, Biosis, Joanna Briggs, Global Health, and World Health Organization COVID-19 database (preprints).

Results: 72 studies met the inclusion criteria, of which 35 evaluated individual public health measures and 37 assessed multiple public health measures as a "package of interventions." Eight of 35 studies were included in the meta-analysis, which indicated a reduction in incidence of covid-19 associated with handwashing (relative risk 0.47, 95% confidence interval 0.19 to 1.12, I2=12%), mask wearing (0.47, 0.29 to 0.75, I2=84%), and physical distancing (0.75, 0.59 to 0.95, I2=87%). Owing to heterogeneity of the studies, meta-analysis was not possible for the

outcomes of quarantine and isolation, universal lockdowns, and closures of borders, schools, and workplaces. The effects of these interventions were synthesised descriptively.

Conclusions: This systematic review and meta-analysis suggests that several personal protective and social measures, including handwashing, mask wearing, and physical distancing are associated with reductions in the incidence covid-19. Public health efforts to implement public health measures should consider community health and sociocultural needs, and future research is needed to better understand the effectiveness of public health measures in the context of covid-19 vaccination."

Clin Microbiol Infect: <u>Transmission of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) from pre and asymptomatic infected individuals.</u> A systematic review (29 October 2021)

"Background: The role of SARS-Cov-2 infected persons who develop symptoms post-testing (presymptomatics) or not at all (asymptomatics) in the pandemic spread is unknown.

Objectives: To determine infectiousness and probable contribution of asymptomatic (at the time of testing) to pandemic SARS-CoV-2 spread.

Data sources: LitCovid, medRxiv, Google Scholar, and WHO Covid-19 databases (to 31 March 2021) and references in included studies.

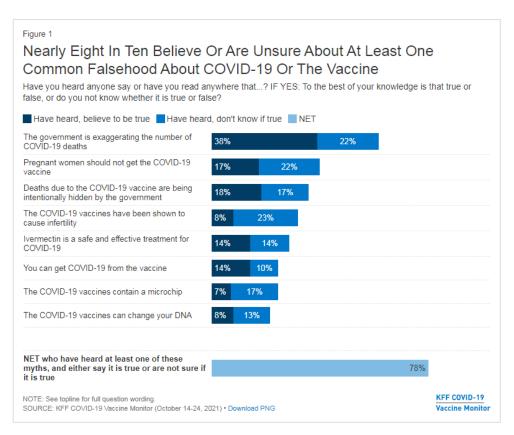
Results: We included 18 studies from a diverse setting with substantial methodological variation (this field lacks standardized methodology). At initial testing, prevalence of asymptomatic cases was 12.5-100%. Of these, 6-100% were later determined to be presymptomatic, this proportion varying according to setting, methods of case ascertainment, and population. Nursing/care home facilities reported high rates of presymptomatic: 50-100% (n=3 studies). Fourteen studies were classified as high risk of, and four studies as at moderate risk of symptom ascertainment bias. High risk studies may be less likely to distinguish between presymptomatic and asymptomatic cases. Six asymptomatic studies and four presymptomatic studies reported culturing infectious virus; data were too sparse to determine infectiousness duration. Three studies provided evidence of possible and three of probable/likely asymptomatic transmission; five studies provided possible and two probable/likely presymptomatic SARS-CoV-2 transmission.

Conclusions: High-quality studies provide probable evidence of SARS-CoV-2 transmission from presymptomatic and asymptomatic individuals, with highly variable estimated transmission rates."

### **Health Messaging and Misinformation**

### News in Brief

-> Figure: "COVID-19 misinformation is ubiquitous: 78% of the public believes or is unsure about at least one false statement, and nearly a third believe at least four of eight false statements tested" (KFF; see also: full report on media and misinformation).



"New data suggests more doctors spending time addressing COVID-19 vaccine misinformation as compared to six months ago" (<u>Sermo</u>; see also: <u>COVID-19 trend reports</u>).

"Alaska doctors plan to ask the State Medical Board to investigate concerns about the spread of misinformation about COVID-19 vaccines and treatments by other physicians" (AP).

File under 'you just can't make this up': "Covid vaccine holdouts are caving to mandates — then scrambling to 'undo' their shots: As mandates spread, anti-vaccine groups have been trafficking in pseudoscience treatments meant to remove or counteract the vaccines" (NBC).

### Long Reads

"Five points for anger, one for a 'like': How Facebook's formula fostered rage and misinformation — Facebook engineers gave extra value to emoji reactions, including 'angry,' pushing more emotional and provocative content into users' news feeds" (WP).

### **Journal Articles**

BMJ Open: What influences people's responses to public health messages for managing risks and preventing infectious diseases? A rapid systematic review of the evidence and recommendations (11 November 2021)

"Background: Individual behaviour changes, such as hand hygiene and physical distancing, are required on a population scale to reduce transmission of infectious diseases such as COVID-19. However, little is known about effective methods of communicating risk reducing information, and how populations might respond.

Objective: To synthesise evidence relating to what (1) characterises effective public health messages for managing risk and preventing infectious disease and (2) influences people's responses to messages.

Results: Sixty-eight eligible papers were identified. Characteristics of effective messaging include delivery by credible sources, community engagement, increasing awareness/knowledge, mapping to stage of epidemic/pandemic. To influence intent effectively, public health messages need to be acceptable, increase understanding/perceptions of health threat and perceived susceptibility.

Discussion: There are four key recommendations: (1) engage communities in development of messaging, (2) address uncertainty immediately and with transparency, (3) focus on unifying messages from sources and (4) frame messages aimed at increasing understanding, social responsibility and personal control. Embedding principles of behavioural science into public health messaging is an important step towards more effective health-risk communication during epidemics/pandemics."

### Other Infectious Diseases and Public Health Issues

## News in Brief

"Maryland state health officials reported Tuesday a single confirmed case of monkeypox virus infection in a Maryland resident who recently returned from Nigeria" (ONT; see also: CDC statement).

Three adults in New Hampshire have tested positive for Jamestown Canyon virus (NH DHHS).

"India's latest Zika outbreak sees surge of nearly 100 cases" (Reuters).

"Vials labeled 'smallpox' found at vaccine research facility in Pennsylvania, CDC says" (CNN).

The University of Oxford is recruiting for a phase I trial of an Ebola vaccine in humans (Oxford).

Be careful with those salads — baby spinach has been linked to an E. coli outbreak (CDC).

#### **Journal Articles**

Ann Intern Med: <u>A Possible Sterilizing Cure of HIV-1 Infection Without Stem Cell Transplantation</u> (16 November 2021)

"Background: A sterilizing cure of HIV-1 infection has been reported in 2 persons living with HIV-1 who underwent allogeneic hematopoietic stem cell transplantations from donors who were homozygous for the CCR5 $\Delta$ 32 gene polymorphism. However, this has been considered elusive during natural infection.

Objective: To evaluate persistent HIV-1 reservoir cells in an elite controller with undetectable HIV-1 viremia for more than 8 years in the absence of antiretroviral therapy.

Design: Detailed investigation of virologic and immunologic characteristics.

Setting: Tertiary care centers in Buenos Aires, Argentina, and Boston, Massachusetts.

Patient: A patient with HIV-1 infection and durable drug-free suppression of HIV-1 replication.

Measurements: Analysis of genome-intact and replication-competent HIV-1 using near-full-length individual proviral sequencing and viral outgrowth assays, respectively; analysis of HIV-1 plasma RNA by ultrasensitive HIV-1 viral load testing.

Results: No genome-intact HIV-1 proviruses were detected in analysis of a total of 1.188 billion peripheral blood mononuclear cells and 503 million mononuclear cells from placental tissues. Seven defective proviruses, some of them derived from clonally expanded cells, were detected. A viral outgrowth assay failed to retrieve replication-competent HIV-1 from 150 million resting CD4+ T cells. No HIV-1 RNA was detected in 4.5 mL of plasma.

Limitations: Absence of evidence for intact HIV-1 proviruses in large numbers of cells is not evidence of absence of intact HIV-1 proviruses. A sterilizing cure of HIV-1 can never be empirically proved.

Conclusion: Genome-intact and replication-competent HIV-1 were not detected in an elite controller despite analysis of massive numbers of cells from blood and tissues, suggesting that this patient may have naturally achieved a sterilizing cure of HIV-1 infection. These observations raise the possibility that a sterilizing cure may be an extremely rare but possible outcome of HIV-1 infection."

Lancet: <u>Safety and immunogenicity of concomitant administration of COVID-19 vaccines</u> (<u>ChAdOx1 or BNT162b2</u>) with seasonal influenza vaccines in adults in the UK (<u>ComFluCOV</u>): a multicentre, randomised, controlled, phase 4 trial (11 November 2021)

"Background: Concomitant administration of COVID-19 and influenza vaccines could reduce burden on health-care systems. We aimed to assess the safety of concomitant administration of ChAdOx1 or BNT162b2 plus an age-appropriate influenza vaccine.

Methods: In this multicentre, randomised, controlled, phase 4 trial, adults in receipt of a single dose of ChAdOx1 or BNT162b2 were enrolled at 12 UK sites and randomly assigned (1:1) to receive concomitant administration of either an age-appropriate influenza vaccine or placebo alongside their second dose of COVID-19 vaccine. 3 weeks later the group who received placebo received the influenza vaccine, and vice versa. Participants were followed up for 6 weeks. The influenza vaccines were three seasonal, inactivated vaccines (trivalent, MF59C adjuvanted or a cellular or recombinant quadrivalent vaccine). Participants and investigators were masked to the allocation. The primary endpoint was one or more participant-reported solicited systemic reactions in the 7 days after first trial vaccination(s), with a difference of less than 25% considered non-inferior. Analyses were done on an intention-to-treat basis. Local and unsolicited systemic reactions and humoral responses were also assessed. The trial is registered with ISRCTN, ISRCTN14391248.

Findings: Between April 1 and June 26, 2021, 679 participants were recruited to one of six cohorts, as follows: 129 ChAdOx1 plus cellular quadrivalent influenza vaccine, 139 BNT162b2 plus cellular quadrivalent influenza vaccine, 146 ChAdOx1 plus MF59C adjuvanted, trivalent influenza vaccine, 79 BNT162b2 plus MF59C adjuvanted, trivalent influenza vaccine, 128 ChAdOx1 plus recombinant quadrivalent influenza vaccine, and 58 BNT162b2 plus recombinant quadrivalent influenza vaccine. 340 participants were assigned to concomitant administration of influenza and a second dose of COVID-19 vaccine at day 0 followed by placebo at day 21, and 339 participants were randomly assigned to concomitant administration of placebo and a second dose of COVID-19 vaccine at day 0 followed by influenza vaccine at day 21. Non-inferiority was indicated in four cohorts, as follows: ChAdOx1 plus cellular quadrivalent influenza vaccine (risk difference for influenza vaccine minus placebos -1·29%, 95% CI -14·7 to 12·1), BNT162b2 plus cellular quadrivalent influenza vaccine (6·17%, -6·27 to 18·6), BNT162b2 plus MF59C adjuvanted, trivalent influenza vaccine (-12.9%, -34.2 to 8.37), and ChAdOx1 plus recombinant quadrivalent influenza vaccine (2.53%, -13.3 to 18.3). In the other two cohorts, the upper limit of the 95% CI exceeded the 0.25 non-inferiority margin (ChAdOx1 plus MF59C adjuvanted, trivalent influenza vaccine 10.3%, -5.44 to 26.0; BNT162b2 plus recombinant quadrivalent influenza vaccine 6.75%, -11.8 to 25.3). Most systemic reactions to vaccination were mild or moderate. Rates of local and unsolicited systemic reactions were similar between the randomly assigned groups. One serious adverse event, hospitalisation with severe

headache, was considered related to the trial intervention. Immune responses were not adversely affected.

Interpretation: Concomitant vaccination with ChAdOx1 or BNT162b2 plus an age-appropriate influenza vaccine raises no safety concerns and preserves antibody responses to both vaccines. Concomitant vaccination with both COVID-19 and influenza vaccines over the next immunisation season should reduce the burden on health-care services for vaccine delivery, allowing for timely vaccine administration and protection from COVID-19 and influenza for those in need."

MMWR: <u>Influenza Vaccinations During the COVID-19 Pandemic — 11 U.S. Jurisdictions, September—December 2020</u> (12 November 2021)

"What is already known about this topic? As the United States enters the 2021–22 influenza season, influenza-associated morbidity and mortality could further strain health care systems already overburdened by the ongoing COVID-19 pandemic.

What is added by this report? During September–December 2020, overall influenza vaccine administration was 9.0% higher than the average during September–December in 2018 and 2019; however, the number of administered doses declined among children aged 6–23 months (13.9%) and 2–4 years (11.9%).

What are the implications for public health practice? Continued strategic efforts are needed to ensure high influenza vaccination coverage among all eligible persons aged ≥6 months, especially children aged ≤4 years."

MMWR: <u>Progress Toward Regional Measles Elimination — Worldwide, 2000–2020</u> (12 November 2021)

"What is already known about this topic? All six World Health Organization (WHO) regions remain committed to measles elimination.

What is added by this report? Annual reported measles incidence decreased globally during 2000–2016, increased in all regions during 2017–2019, then decreased in 2020. Measles surveillance, already suboptimal, worsened in 2020. Since 2000, estimated measles deaths decreased 94%. Measles vaccination has prevented an estimated 31.7 million deaths worldwide. No WHO region has achieved and maintained measles elimination.

What are the implications for public health practice? To achieve regional measles elimination targets, enhanced efforts are needed to reach all children with 2 doses of measles-containing vaccine, implement robust surveillance, and identify and close immunity gaps."

Int Health: <u>The underrepresentation of palliative care in global guidelines for responding to infectious disease outbreaks: a systematic narrative review</u> (09 November 2021)

"Background: The importance of palliative care provision has been highlighted in previous humanitarian emergencies. This review aimed to examine the breadth and depth of palliative care inclusion within global guidelines for responding to infectious disease outbreaks.

Methods: The review was conducted using the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines. Electronic searches of MEDLINE, Embase, Cumulative Index to Nursing and Allied Health, PsychInfo and grey literature were performed. Inclusion criteria were guidelines (recommendations for clinical practice or public health policy) for responding to infectious disease outbreaks in the general adult population. Results were limited to the English language, between 1 January 2010 and 17 August 2020. Analysis of the included articles involved assessing the breadth (number of palliative care domains covered) and depth (detail with which the domains were addressed) of palliative care inclusion.

Results: A total of 584 articles were retrieved and 43 met the inclusion criteria. Two additional articles were identified through handsearching. There was limited inclusion of palliative care in the guidelines examined.

Conclusions: There is an opportunity for the development of guidelines that include information on palliative care implementation in the context of infectious disease outbreaks in order to reduce the suffering of key vulnerable populations worldwide."

#### **Statistics**

	Total Cases	Total Deaths	Total Vaccine Doses Administered				
Global	256,279,320	5,136,072	7,613,975,278				
United States	47,533,739	768,717	444,383,181				
IHIL CSSE as of 1000 EDT 10 No							

JHU CSSE as of 1000 EDT 19 November 2021

Virginia	Total cases (state)	Chesapeake	Hampton	Newport News	Norfolk	Portsmouth	Suffolk	Virginia Beach
Cases	953,460	29,390	15,345	21,001	24,868	12,884	11,139	50,806
Hospitalizations	39,684	1,331	706	801	1,537	931	709	2,651
Deaths	14,492	368	244	304	355	248	244	568

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